

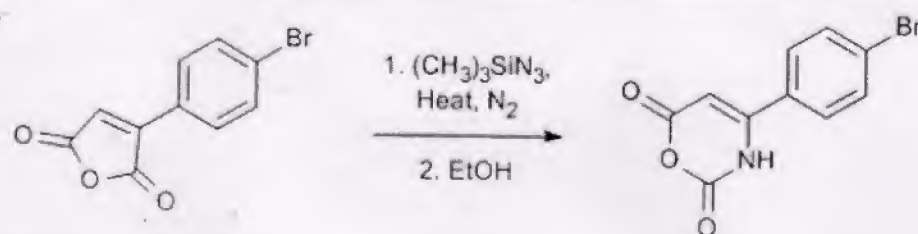
Nitrogen insertion reaction of trimethylsilyl azide with aryl substituted maleic anhydrides, yielding aryl substituted 1,3(3H) oxazine-2,6-diones; 4-(4-bromophenyl)-1,3(3H) oxazine-2,6-dione

SyntheticPage 526

DOI: 10.1039/SP526

Submitted Dec 23, 2011, published Jan 16, 2012

John MacMillan (john.macmillan@temple.edu)



Chemicals Used

4-bromophenyl maleic anhydride
Trimethylsilylazide (Sigma Aldrich)
Dioxane (Sigma Aldrich)
Toluene (Sigma Aldrich)
Ethanol (Sigma Aldrich)

Procedure

A 50 ml 3 neck round bottom flask, equipped with water condenser, heating mantle, dropping funnel, nitrogen inlet, magnetic stirrer, and calcium chloride drying tube, was charged under nitrogen with 4.75g (0.019 mole) 4-bromophenyl maleic anhydride, 12ml (~ 0.09 mole) trimethylsilyl azide, and 3 ml dry dioxane. A rubber tube exiting the water condenser lead to a one liter water filled inverted graduate cylinder in a water trough, allowing for easy monitoring of nitrogen evolution. The mixture was refluxed 3 hrs after which nitrogen gas evolution ceased. TLC (silica gel, ethyl acetate eluent) showed primarily the 4- isomer with traces of the 5-isomer. The solution was cooled in ice to 0 °C and 40 ml toluene was added with stirring. Addition of 1 ml ethanol gave a copious white precipitate which TLC showed to be pure 4-isomer. The precipitate was suction filtered and mother liquor concentrated further, giving 2.9g (58%), 4-(4-bromophenyl)-1,3(3H) oxazine-2,6-dione in three crops. Recrystallization of a small sample from ethyl acetate gave white crystals,

Author's Comments

Trimethylsilylazide is toxic and must always be handled in a fume hood. Never allow azide wastes to contact heavy metal, as explosive azide salts may result

Additional unreported aryl substituted 1,3(3H) oxazine-2,6-diones were synthesized by essentially the procedure above in similar yields, and converted to their N-alkylated derivatives by refluxing the corresponding aryl substituted oxauracil with a di-alkyl sulfate/sodium bicarbonate slurry in acetone, as described in the lead reference.

See <http://furlip.solidwebhost.com/aryloxauracils.htm>

Data

m.p. 207-209 °C (dec).

Anal. Calc. For $C_{10}H_6BrNO_3$: C, 44.80, H, 2.26, N, 5.23, Br, 29.81.

Found: C, 44.74, H, 2.17, N, 5.18, Br, 29.79. Satisfactory

Ir, (mull), 3220(w), 3160(w), 3100 (w), 1790(s), 1800(s), 1710(s), 1630(s), 1595(m), 1500(m), 1400(w), 1305(w), 1270(w), 1220(w) 1110(m), 1085(m), 1070(m), 1005(w), 980(m), 840(m), 805(m), 750 (m) cm^{-1} .

1H NMR (DMSO- d_6 , 60mz), δ 7.7(broad singlet, 4H, aromatics), 6.0 (s, 1H, N-H), 5.66 (s, 1H, C5-H).

Lead Reference

J.H. MacMillan and S.S. Washburne, J. Heterocyclic Chemistry, Vol. 12, p 1215, (1975)

Other References

James D. Warren, John H. MacMillan and Stephen S. Washburne, J. Org. Chem., Vol 40, p 375 (1975).

Keywords: amination, aromatics/arenes, electrophilic, elimination, heterocyclic compounds, insertion, nucleosides, thermal